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9659 U.S. PAT.
OFF.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

DIVISIONAL APPLICATION REQUEST TRANSMITTAL

ASSISTANT COMMISSIONER OF PATENTS
Washington, D.C. 20231
S I R:

Attorney Docket No. XI/P03139US2

Prior Application Information:

Art Unit: 1615

Examiner: N. Levy

Serial No.: 08/863,182

Transmitted herewith for filing is a **Rule 53(b) Divisional** patent application

of: JEANNIN, Philippe

for: N-PHENYLPYRAZOLE-BASED ANTI-FLEA AND ANTI-TICK COLLAR FOR CATS AND DOGS.

ENCLOSED are the following:

1. [XX] Specification, abstract and claims of 32 pages.
2. [XX] sheets of [] formal [] informal drawings [XX] No drawings.
3. [XX] Declaration (original or copy) signed by the named inventor.
4. [XX] Preliminary Amendment
5. [] Information Disclosure Statement
6. [] Other:

NOTE the following:

7. [] Applicant is a small entity, which was established in parent application Serial No. *, and such status is still proper and desired.
8. [XX] The prior application is assigned to RHONE MERIEUX.
9. [XX] Priority of the following applications are claimed under 35 U.S.C. 119:

Serial No.	Date Filed	Country	Certified Copy of Priority Doc. Filed	
			in USSN	Date
96 04 206	29 March 1996	France	08/863,182	May 27, 1997
96 03 707	26 March 1997	France	08/863,182	December 17, 1997

10. [XX] Amend the specification by inserting before the first line the sentence:
 - a. [] This is a continuation of application Serial No. * filed *.
 - b. [XX] This is a divisional of application Serial No. 08/863,182 filed May 27, 1997; which is a CIP of 08/692,430 filed 08/05/96 now abandoned.

1549 U.S. PTO
09/17/4598
10/19/98

11. [] Cancel claims prior to calculation of the filing fee.

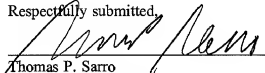
FILING FEE: calculated below (after reduction for amendment or claims cancellations if noted above):

[X] Total claims:	50	-	20	=	30	x	\$ 22.00	=	\$ 660.00
[X] Independent claims:	3	-	3	=	0	x	\$ 82.00	=	\$
[] Multiple dependent claim(s)						+	\$270.00	=	\$
							BASIC FEE	=	<u>\$ 790.00</u>
							TOTAL OF ABOVE CALCULATIONS	=	\$
[] Reduction by 1/2 for filing by small entity								=	<u>\$[]</u>
							SUBTOTAL	=	\$1,450.00
[] Fee for extension of time in parent application								+	<u>\$</u>
TOTAL OF FEES								=	\$1,450.00

[XX] A check in the amount of \$1,450.00 is enclosed (must at least cover the basic fee). If no check or an insufficient check is enclosed and a fee is due herewith, the Commissioner is authorized to charge any fee or additional fee due in connection herewith to Deposit Account No. 12-0555. A duplicate of this sheet is enclosed.

[XX] In the event that a petition for extension of time is required to be submitted in the pending prior application, and in the event that a separate petition for the pending prior application is not filed on even date, applicant hereby petitions under 37 C.F.R. §1.136(a) for an extension of time in the pending prior application of as many months as are required to render this submission timely. The Commissioner is authorized to charge any fee or additional fee due in connection with this communication to Deposit Account No. 12-0555. A duplicate copy of this sheet is enclosed.

Respectfully submitted,


Thomas P. Sarro
Registration No. 19,396

Date: October 19, 1998

LARSON & TAYLOR • Suite 900 • 1199 North Fairfax St. • Alexandria, VA 22314

Rule 53(b) Divisional Application Filed Concurrently Herewith

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Attorney's Docket: XI/P03139US2

JEANNIN, Philippe

Divisional Application of

Serial No. 08/863,182

: Art Unit: 1615

Filed: Concurrently herewith

: Examiner: N. Levy

For: N-PHENYLPYRAZOLE-BASED ANTI-FLEA AND ANTI-TICK COLLAR FOR CATS
AND DOGS

PRELIMINARY AMENDMENT

The Assistant Commissioner of Patents
Washington, D.C.

S I R:

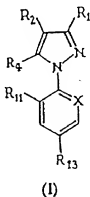
Preliminary to examination of the above-identified application, please amend the
application as follows:

IN THE CLAIMS

Please amend claim 1 as follows:

1. (Amended) Anti-flea and anti-tick [collar or other] external device for a pet,
[in particular a cat or dog, made of] to ensure more than six months of efficacy of greater
than 95% against fleas, as determined in a test providing the reinfestation of the pet with

100 ± 10 fleas, and more than three months of efficacy of greater than 90% against ticks, as determined in a test providing the reinfestation of the pet with 50 ± 3 three ticks, comprising a matrix in which is incorporated from 0.1 to 40% by weight, relative to the [collar] external device, of a substance which is active against fleas and ticks, this active substance being formed of at least one compound corresponding to formula (I) below



in which:

R_1 is CN or methyl or a halogen atom;

R_2 is $S(O)_nR_3$ or 4,5-dicyanoimidazol-2-yl or haloalkyl;

R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical NR_5R_6 , $S(O)_mR_7$, $C(O)R_7$, $C(O)O-R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)$ (R_{10});

R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, $C(O)$ alkyl, alkoxy carbonyl or $S(O)_nCF_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

R_7 represents an alkyl or haloalkyl radical;

R₈ represents an alkyl or haloalkyl radical or a hydrogen atom;

R₉ represents an alkyl radical or a hydrogen atom;

R₁₀ represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

R₁₁ and R₁₂ represent, independently of each other, a hydrogen or halogen atom, or CN or NO₂;

R₁₃ represents a halogen atom or a haloalkyl, haloalkoxy, S(O)_qCF₃ or SF₅ group;

m, n, q and r represent, independently of each other, an integer equal to 0, 1 or 2;

X represents a trivalent nitrogen atom or a radical C-R₁₂, the other three valency positions of the carbon atom forming part of the aromatic ring;

with the proviso that when R₁ is methyl, either R₃ is haloalkyl, R₄ is NH₂, R₁₁ is Cl, R₁₃ is CF₃ and X is N; or R₂ is 4,5-dicyanoimidazol-2-yl, R₄ is Cl, R₁₁ is Cl, R₁₃ is CF₃, and X is =C-Cl[;]

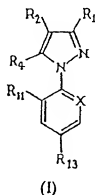
[this collar or other external device being designed to ensure more than 6 months of efficacy against fleas and more than 3 months of efficacy against ticks, the efficacy preferably being maintained for several weeks even if the collar or other external device is taken off or lost or if there is a variation in the release of the compound (I) by the matrix].

Please add the following new claims 48-52:

--48. Anti-flea and anti-tick device according to claim 1 wherein the device ensures more than six months of efficacy against fleas and more than three months of efficacy against ticks.

49. Method for eliminating fleas and ticks from cats and dogs comprising:

attaching to the cats and dogs at least one external device which comprises a matrix incorporating from 0.1 to 40% by weight, relative to the [collar] external device, of a substance which is active against fleas and ticks, this active substance being formed of at least one compound corresponding to formula (I) below



in which:

R_1 is CN or methyl or a halogen atom;

R_2 is $S(O)_n R_3$ or 4,5-dicyanoimidazol-2-yl or haloalkyl;

R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical $NR_5 R_6$, $S(O)_m R_7$, $C(O)R_7$, $C(O)O-R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9) (R_{10})$;

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R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, C(O)alkyl, alkoxycarbonyl or S(O)_qCF₃ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

R_7 represents an alkyl or haloalkyl radical;

R_8 represents an alkyl or haloalkyl radical or a hydrogen atom;

R_9 represents an alkyl radical or a hydrogen atom;

R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom, or CN or NO₂;

R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, S(O)_qCF₃ or SF₅ group;

m , n , q and r represent, independently of each other, an integer equal to 0, 1 or 2;

X represents a trivalent nitrogen atom or a radical C- R_{12} , the other three valency positions of the carbon atom forming part of the aromatic ring;

with the proviso that when R_1 is methyl, either R_3 is haloalkyl, R_4 is NH₂, R_{11} is Cl, R_{13} is CF₃ and X is N; or R_2 is 4,5-dicyanoimidazol-2-yl, R_4 is Cl, R_{11} is CL, R_{13} is CF₃, and X is =C-Cl;

allowing external device to remain in place in order for compound (I) to be taken up by the animal's sebum and distributed over the animal's entire body, and to be concentrated in the sebaceous glands which become a reservoir for formula (I),

in such a manner that it ensures more than six months of efficacy of more than 95% against fleas, as determined in a test providing reinfestation with 100 ± 10 fleas, and more than three months of efficacy of greater than 90% against ticks, as determined in a test providing reinfestation with 50 ± 3 ticks, and that one obtains efficacy during several weeks against ticks and fleas, if the collar or other external is taken off or lost and if there is a variation in the rate of release of the formula (I) by the matrix.

50. Method according to claim 49, wherein the external device is left in place for at least 24 hours.

51. Method according to claim 49, wherein one obtains an efficacy of two to three months against fleas if the external device is taken off or lost or if there is a variation in the rate of release of the formula (I) by the matrix.

52. Method according to claim 49, wherein one obtains an efficacy of one to two months against ticks if the external device is taken off or lost or if there is a variation in the rate of release of the formula (I) by the matrix.--

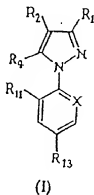
Please cancel claim 12 on page 26, lines 22 and 23.

Please cancel claims 39 and 41 without prejudice.

Please amend the claims as follows:

Claim 11, line 5, delete "and its derivatives".

21. (Amended) Method for eliminating fleas and ticks from pets to ensure more than six months of efficacy of greater than 95% against fleas, as determined in a test providing the reinfestation of the pet with 100 ± 10 fleas, and more than three months of efficacy of greater than 90% against ticks, as determined in a test providing the reinfestation of the pet with 50 ± 3 three ticks., [in particular cats and dogs, in which one attaches] comprising attaching to the pets at least one [collar or other] external device [which comprises] having a matrix into which is incorporated a compound corresponding to formula (I) below:



in which:

R_1 is CN or methyl or a halogen atom;

R_2 is $S(O)_nR_3$ or 4,5-dicyanoimidazol-2-yl or haloalkyl;

R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical NR_5R_6 , $S(O)_mR_7$, $C(O)R_7$, $C(O)O-R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)$ (R_{10});

R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, $C(O)$ alkyl, alkoxycarbonyl or $S(O)_nCF_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

R_7 represents an alkyl or haloalkyl radical;

R_8 represents an alkyl or haloalkyl radical or a hydrogen atom;

R_9 represents an alkyl radical or a hydrogen atom;

R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom, or CN or NO_2 ;

R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, $S(O)_qCF_3$ or SF_5 group;

m, n, q and r represent, independently of each other, an integer equal to 0, 1 or 2;

X represents a trivalent nitrogen atom or a radical C-R₁₂, the other three valency positions of the carbon atom forming part of the aromatic ring;

with the proviso that when R₁ is methyl, either R₃ is haloalkyl, R₄ is NH₂, R₁₁ is Cl, R₁₃ is CF₃ and X is N; or R₂ is 4,5-dicyanoimidazol-2-yl, R₄ is Cl, R₁₁ is Cl, R₁₃ is CF₃, and X is =C-Cl[:]

[which method ensuring prevention and treating fleas and ticks to a high degree of efficacy and other a period exceeding 6 months against fleas and 3 months against ticks, the efficacy preferably being maintained over several weeks even if the collar or external device is taken off or if there is a variation in the release of the compound (I) by the collar or the external device].

- | | | |
|-----------|------------|---|
| Claim 31, | line 5, | delete "and its derivatives. |
| Claim 32, | line 2, | delete "proportion" and insert --concentration--. |
| Claim 33, | line 2, | delete "proportion" and insert --concentration--. |
| Claim 34, | line 2, | delete "proportion" and insert --concentration--. |
| Claim 35, | line 2, | delete "proportion" and insert --concentration--. |
| Claim 36, | line 2, | delete "proportion" and insert --concentration--. |
| Claim 37, | line 2, | delete "proportion" and insert --concentration--. |
| Claim 38, | line 2, | delete "proportion" and insert --concentration--. |
| Claim 44, | lines 1-2, | delete "long-lasting". |
| Claim 45, | lines 1-2, | delete "long-lasting". |

Claim 46, lines 1-2, delete "long-lasting".

Claim 47, line 2, delete "collar or".

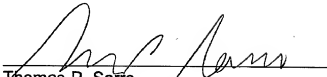
REMARKS

Entry of the above amendment is respectfully requested.

Respectfully submitted,

LARSON AND TAYLOR

Date: October 19, 1998


Thomas P. Sarfo
Registration No. 19,396

Suite 900
1199 North Fairfax Street
Alexandria, Virginia, 22314
(703) 739-4900

**N-Phenylpyrazole-based anti-flea and anti-tick collar
for cats and dogs**

5 The present invention relates to an external antiparasitic device, in particular a collar, for pets, in particular cats and dogs, this collar being active against the ectoparasites of these animals, in particular fleas and ticks.

10 The invention also relates to the use of active compounds for the manufacture of such collars or external devices, as well as to a treatment process relating thereto.

15 The invention is directed mainly towards fleas of the genus *Ctenocephalides*, in particular *C. felis* and *C. canis*, and ticks, in particular of the genus *Rhipicephalus*, especially *sanguineus*, as well as harvest ticks (*Trombicula autumnalis*), which are acarids that mainly attack hunting dogs.

20 Collars intended to eliminate common ectoparasites from cats and dogs have been produced for a long time. These collars consist of a matrix, usually a plastic matrix, which incorporates between 5 and 40% active substance and is capable of releasing it over
25 time. These collars thus theoretically have the aim of ensuring long-lasting protection.

 However, despite the activity claims, out in the field the collars do not have the efficacy required to ensure the actual elimination of these parasites. The
30 cause of this may be the low activity of the active substance included in the matrix. Another cause may be

the accelerated degradation of these active substances under the effect of climatic factors, such as light, heat and rain. Lastly, control of the release of the active substance from the matrix is largely overevaluated. Release generally proves to be difficult and variable, and may depend greatly on the manufacturing conditions, which may vary from one batch to another, and on the conditions of use, in particular climatic variations and especially humidity and temperature, etc. In addition, only a relatively small amount of the active substance incorporated is actually released and it proves difficult to be able to control and optimize its release.

Another drawback of the collars encountered in practice arises from the mode of use of this device which may, obviously, be taken off, worn irregularly, or even be pulled off when the animal moves about, for example in undergrowth; the problem is particularly critical for hunting dogs whose collars are removed before a hunting outing even though they will be confronted with a flea- and tick-ridden environment.

Patent applications WO-A-87/03781 and EP-A-0,295,117 have proposed insecticides of the N-phenylpyrazole class.

These substances are described as being active against a very large number of parasites encountered in various fields, namely agriculture, public health and human and veterinary medicine. In the latter field, these substances may act in particular against the fleas and ticks of pets, such as cats and dogs. These substances may be applied in various ways, namely via the oral, parenteral, percutaneous or topical route. The latter type of administration itself covers many

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possibilities, namely sprays, powders, baths, showers, jets, greases, shampoos, creams, waxes, preparations of skin solution type (pour-on) and external devices such as earrings and collars to provide local or systemic treatment. EP-A-0,295,117 and EP-A-0,500,209 propose a slow release composition which may be in the form of a collar or earrings for controlling harmful insects. Such a formulation may comprise from 0.5% to 25% active material, from 75 to 99.5% polyvinyl chloride and a catalytic amount of a plasticizer, dioctyl phthalate.

French patent application FR-A-2,713,889 describes a pesticide composition containing an insect growth regulator and an N-aryldiazole derivative chosen from the derivatives 4-(2-bromo-1,1,2,2-tetrafluoroethyl)-1-(3-chloro-5-trifluoromethylpyridine-2-yl)-2-methylimidazole, 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinyldipyrzole and 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole. As in the prior documents discussed above, the compositions are directed towards a large number of insects in different fields, and various types of formulations. Dog fleas and cat fleas are targeted. Among the formulations proposed, this document mentions resinous preparations which may be made into pesticide collars for animals.

However, none of these documents describes the use of pesticidal collars comprising a compound of the N-phenylpyrazole family to control fleas and ticks on pets such as cats and dogs, which make it possible to ensure a high level of efficacy for a long period against these parasites.

As for the pesticidal compounds of the prior art, a specialist might have expected to encounter

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conventional problems of release from the collars and thus problems of activity.

After all, French patent application FR-A-2,713,889 proposes, does it not, the combination of such
5 compounds with an insect growth regulator?

The publications C. Genchi et al., Professione Veterinaria No. 1, supplement 1995, pages 19 to 22, J.M. Postal, Professione Veterinaria No. 1, supplement 1995, pages 17 and 18 and A. Searle et al., Australian Veterinary Practitioner, volume 25, No. 3, 1995,
10 pages 157 and 158 propose instead to effectively control fleas and ticks using a sprayable solution (spray) containing this type of active compound.

The Applicant has now found, surprisingly,
15 that despite the fact that these N-phenylpyrazoles encounter the same difficulties of release as the products of the prior art, it is however possible to obtain collars which are entirely effective for the elimination of cat and dog ectoparasites over a very long period,
20 for example from 6 to 18 months, and that, in addition, the efficacy persists long after the collar is taken off, namely over a period which may be equal to or exceed 2 months, such that it is then possible to obtain a collar which is entirely effective irrespective of the
25 conditions of use. On account of the fact that the protection persists after the collar is taken off, it may be understood that irregular or voluntary use or that resulting from loss of the collar does not jeopardize the protection from which the animal should benefit.
30

In addition, the Applicant has observed that this long-lasting efficacy was obtained with concentrations of active substance in the matrix forming the

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collar which were much smaller than those of the standard products. It was also observed that this efficacy was obtained within a very short time of the collars being put on, in particular an efficacy of greater than
5 95% in 24 h against fleas and greater than 90% in 48 h against ticks.

It was observed, very surprisingly, that the compounds according to the invention, which are very
lipophilic and of high vapour pressure (low volatility),
10 had a very high affinity for the sebum which usually covers the animal's coat (skin and hair), such that, when released, this compound is taken up by the sebum, after which a translocation phenomenon occurs ensuring distribution of active substance over the animal's
15 entire body. In addition, and this is a noteworthy point, these active substances become concentrated in the sebaceous glands which become a reservoir for them, ensuring very long-lasting efficacy and making it possible to compensate for the absence of the collar, by releasing the active substance by passive diffusion.
20

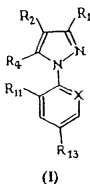
By virtue of this phenomenon, the variations in release of the active substance by the collar on account of, for example, a variation in climatic conditions, are compensated for by the possibilities of
25 release by the sebaceous glands.

It was also observed that after a bath, which could possibly lead to the removal of the sebum distributed over the animal's body, the animal very rapidly became reprotected, in the presence or absence
30 of the collar, owing to the fact that secretion of new sebum is accompanied by a release, by the sebaceous glands, of the active substance that they contain.

The subject of the present invention is thus

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a collar or other external device for a pet, in particular a cat or dog, made of a matrix in which is incorporated from 0.1 to 40% by weight, relative to the collar, of a substance which is active against ectoparasites such as fleas and ticks (anti-flea and anti-tick collar or other external device), this active substance being formed of at least one compound corresponding to formula (I) below:



in which:

R_1 is CN or methyl or a halogen atom;

R_2 is $S(O)_n R_3$ or 4,5-dicyanoimidazol-2-yl or haloalkyl;

R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical $NR_5 R_6$, $S(O)_n R_7$, $C(O)R_7$, $C(O)O-R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)(R_{10})$;

R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, $C(O)alkyl$, alkoxy carbonyl or $S(O)_2 CF_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

R_7 represents an alkyl or haloalkyl radical;

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R_9 represents an alkyl or haloalkyl radical or a hydrogen atom;

R_9 represents an alkyl radical or a hydrogen atom;

5 R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom, or optionally CN or
10 NO_2 ;

R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, $\text{S(O)}_q\text{CF}_3$ or SF_3 group;

m , n , q and r represent, independently of each other, an integer equal to 0, 1 or 2;

15 X represents a trivalent nitrogen atom or a radical C-R_{12} , the other three valency positions of the carbon atom forming part of the aromatic ring;

 with the proviso that when R_1 is methyl, either R_3 is haloalkyl, R_4 is NH_2 , R_{11} is Cl, R_{13} is CF_3 and X is N; or R_2 is 4,5-dicyanoimidazol-2-yl, R_4 is Cl, R_{11} is Cl, R_{13} is CF_3 and X is $=\text{C-Cl}$;

 this collar or other external device being designed to ensure at least more than 6 months of efficacy against fleas and at least more than 3 months
25 of efficacy against ticks, the efficacy preferably being maintained for several weeks even if the collar or other external device is taken off or lost or if there is a variation in the rate of release of the compound (I) by the matrix.

30 Preferably, in formula (I),
 R_1 is CN or methyl;
 R_2 is $\text{S(O)}_n\text{R}_3$;
 R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical NR_5R_6 , $S(O)_mR_7$, $C(O)R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)(R_{10})$;

5 R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, $C(O)alkyl$ or $S(O)_lCF_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

10 R_7 represents an alkyl or haloalkyl radical;
 R_8 represents an alkyl or haloalkyl radical or a hydrogen atom;

R_9 represents an alkyl radical or a hydrogen atom;

15 R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom;

20 R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, $S(O)_qCF_3$ or SF_5 group;

m, n, q and r represent, independently of each other, an integer equal to 0, 1 or 2;

25 X represents a trivalent nitrogen atom or a radical $C-R_{12}$, the other three valency positions of the carbon atom forming part of the aromatic ring;

with the proviso that when R_1 is methyl, then R_3 is haloalkyl, R_4 is NH_2 , R_{11} is Cl, R_{13} is CF_3 and X is N.

30 Compounds of formula (I) in which R_1 is CN will be selected most particularly. The compounds in which R_2 is $S(O)_lR_3$, preferably with $n = 1$, R_3 preferably being CF_3 or alkyl, for example methyl or ethyl, or alternatively $n = 0$, R_3 preferably being CF_3 , as well as

those in which $X = C-R_{12}$, R_{12} being a halogen atom, will also be selected. Compounds in which R_{11} is a halogen atom and those in which R_{13} is haloalkyl, preferably CF_3 , are also preferred. In the context of the present invention, compounds combining two or more of these characteristics will advantageously be selected.

A preferred class of compounds of formula (I) consists of compounds such that R_1 is CN , R_3 is haloalkyl, preferably CF_3 , or ethyl, R_4 is NH_2 , R_{11} and R_{12} are, independently of each other, a halogen atom, and/or R_{13} is haloalkyl.

In the present invention, the alkyl radicals may contain generally from 1 to 6 carbon atoms. The cycle formed by the divalent alkylene radical representing R_5 and R_6 , as well as with the nitrogen atom to which R_5 and R_6 are linked may be generally a cycle of 5, 6 or 7 links.

A compound of formula (I) which is most particularly preferred in the invention is

1-[2,6- Cl_2 ,4- CF_3 phenyl]3- CN 4-[SO- CF_3]5- NH_2 pyrazole,
which is referred to hereinbelow as compound A.

Mention may also be made of the two compounds which differ from the above A by the following characteristics:

1- $n = 0$, $R_3 = CF_3$

2- $n = 1$, $R_3 = ethyl$.

Compounds of formula (I) may be prepared according to one or other of the processes described in patent applications WO-A-87/3781, 93/6089, 94/21606 or European patent application EP-A-0,295,117, or any other process falling within the competence of a specialist skilled in the art of chemical synthesis. For the

chemical preparation of the products of the invention, a person skilled in the art is considered as having at his disposal, inter alia, all of the contents of "Chemical Abstracts" and the documents which are cited therein.

However, low concentrations, of from 1 to 15% by weight and more particularly, especially for compound A, of from 1.25 to 10%, are preferred.

Under optimum conditions, compound (I) and especially compound A is present in the collar in a proportion of from 2 to 6% by weight, more particularly from 2.5 to 5% by weight.

It would obviously be possible to add to compound A any other insecticide which might be considered useful.

These insecticides may be present in the same matrix as the compound according to the invention. A composite collar made of at least two parts, each including a different active substance, may also be used.

Within the scope of the invention, matrices usually used to make collars may be used. Preferred examples which may be mentioned are matrices based on PVC (polyvinyl chloride), as described in US-A-3,318,769, 3,852,416 and 4,150,109 and 5,437,869, and other vinyl polymers.

The plasticizers may be chosen in particular from adipates, phthalates, phosphates and citrates.

One or more plasticizers will preferably be added to the PVC, these plasticizers being chosen in particular from the following compounds:

- diethyl phthalate
- dioctyl sebacate

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- dioctyl adipate
- diisodecyl phthalate
- acetyl tributyl citrate
- diethyl hexyl phthalate
- 5 - di-n-butyl phthalate
- benzyl butyl phthalate
- acetyl tributyl citrate
- tricresyl phosphate
- 2-ethylhexyl diphenyl phosphate.

10 Even more preferably, a PVC matrix will be used in the presence of a primary remanent plasticizer and a secondary plasticizer, in particular according to EP-A-0,539,295 and EP-A-0,537,998.

15 Among the secondary plasticizers, mention may be made of the following products:

- acetyl triethyl citrate
- triethyl citrate
- triacetin
- diethylene glycol monoethyl ether
- 20 - triphenyl phosphate.

A common stabilizer may also be added thereto.

For the purposes of the present invention, the term external device should be understood to refer
25 to any device which can be attached externally to the animal in order to provide the same function as a collar.

By varying the concentration and/or composition of the matrix, collars or other external
30 devices according to the invention, which ensure effective and long-lasting protection against fleas, may be made. Collars or other external devices may be made with an efficacy of greater than 6 months, in particular

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of greater than or equal to 12 or 18 months, even when the collar or external device is taken off for a relatively prolonged period. When the collar or device is taken off, the duration of effective protection may range from 2 to 3 months.

By varying the concentration and/or composition of the matrix, it is possible to make collars or other external devices according to the invention which ensure effective and long-lasting protection against ticks. Collars or external devices may be made with an efficacy of greater than 3 months, in particular of greater than or equal to 12 or 15 months, even when the collar or external device is taken off for a relatively prolonged period. When the collar or external device is taken off, the duration of effective protection may range from 1 to 2 months.

It is noteworthy that this very long-lasting and total efficacy is obtained by the compound according to the invention alone, without addition of another insecticide.

The subject of the present invention is also a method for eliminating ectoparasites, in particular fleas and ticks, from pets such as cats and dogs, in which method at least one collar or other external device in accordance with the invention is attached to the animal and the animal is afforded long-lasting, effective protection against these parasites, even when the collar or other external device is taken off. The method is capable of ensuring prevention and treating fleas and ticks to a high degree of efficacy and over a period exceeding 6 months against fleas and 3 months against ticks, the efficacy preferably being maintained over several weeks even if the collar or external device

is taken off or if there is a variation in the release of the compound (I) by the collar or external device. The indications of duration have been given above. Preferably, it is recommended that, in accordance with the method according to the invention, after it has been put on for the first time, the collar or external device should remain on the animal for at least 24 hours in order for sufficient active substance to pass to the animal and for the sebaceous glands to have been able to store this active substance.

The object of this method is non-therapeutic and in particular relates to the cleaning of animal hairs and skin by elimination of the parasites which are present, as well as their residues and dejections. The treated animals thus have hair which is more pleasant to look at and to feel.

The invention also relates to such a method for therapeutic purposes, intended to treat and prevent parasitoses having pathogenic consequences.

The subject of the present invention is also the use of a compound corresponding to formula I for the production of a collar or other external device intended to be attached to a pet, in particular cats and dogs, this compound being capable of ensuring prevention and treating fleas and ticks to a high degree of efficacy and over a period exceeding 6 months against fleas and 3 months against ticks, the efficacy preferably being maintained for several weeks if the collar or the external device is taken off or lost or if there is a variation in the release of the compound (I) by the collar or the external device. The devices as above are concerned.

In particular, the method and device accor-

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ding to the invention are designed to provide for an efficacy of greater than 95%, or even greater than 98 or 99% against fleas.

For ticks, the desired efficacy exceeds 80%
5 or 90%.

Similarly, the invention, against fleas, is directed towards the production of a long-lasting efficacy, longer than or equal to 12 months and even to 18 months.

For ticks, this duration is longer than 12 months, or even longer than 15 months.

Also preferably, the invention is directed towards the production of collars or other external devices which make it possible to obtain an efficacy maintained in the absence of the collar or external
15 device over a period ranging from 2 to 3 months, or more, against fleas and from 1 to 2 months, or more, against ticks.

The present invention will now be described in greater detail with the aid of non-limiting examples from which other particular features and advantages of
20 the invention will emerge.

EXAMPLE 1:

Collar containing 10% compound A

25 The following two types of collar were prepared (mixing and then extrusion):

Formulation 1:	PVC	50.0%
	Stabilizer	0.5%
	Epoxidized soybean oil	5.0%
30	Diisooctyl adipate	34.5%
	Compound A	10.0%
Formulation 2:	PVC	50.0%
	Stabilizer	0.5%

Epoxidized soybean oil . . . 5.0%
2-Ethylhexyl diphenyl
phosphate 34.5%
Compound A 10.0%

5 (% by weight).

For the tests, 9 adult dogs which had not received any insecticide or acaricide for at least 40 days were chosen. The dogs were washed with an insecticide-free shampoo and combed in order to remove any existing parasites.

The dogs were divided into groups of three.

Group A:

Untreated controls

Group B:

15 Collar containing 10% compound A - formulation 1.

Group C:

Collar containing 10% compound A - formulation 2.

The dogs are infested with about 100 ± 10 Ctenocephalides felis cat fleas (Unfed cat fleas) and

20 50 ± 2 Rhipicephalus sanguineus ticks (Brown dog tick).

The treatment follows the following general schema:

DAY

-2 Infestation with the fleas and ticks.

0 Collars are put on.

25 2 Fleas and ticks are counted with a comb.

7 Infestation with ticks.

8 Infestation with fleas.

9 Counting with a comb

35 Infestation with ticks.

30 36 Infestation with fleas.

37 Counting with a comb.

63 Infestation with ticks.

64 Infestation with fleas.

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65 Counting with a comb.

The same process is continued with infestation with fleas and ticks every month for as long as a satisfactory efficacy is observed.

5 Hair samples were taken on:

D 205 and D 261 for all the dogs;

The collars were taken off on D 149 on dogs 363 and 289, on D 177 for dogs 87 and 300 and on D 205 for dogs 256 and 335.

10 The concentrations of active substance according to the invention on the hairs which were obtained at D 205 and D 261 are presented in Tables 1 and 2 respectively, in $\mu\text{g/g}$ of hair.

15 **Table 1: Concentration of active substance according to the invention on D 205.**

DOG	No.	CONCENTRATION ($\mu\text{g.g}^{-1}$)				
		UNDER THE COLLAR	RIGHT FLANK	LEFT FLANK	MIDDLE OF BACK	LUMBAR REGION
20	GROUP B					
	363	18.63	3.11	2.33	1.73	6.99
	87	19.03	2.28	3.08	5.81	4.54
	256	14.66	3.04	3.01	2.48	10.99
25	GROUP C					
	289	27.47	11.75	15.19	8.99	30.9
	300	482.4	34.6	15.69	17.97	36.7
	335	257.4	23.86	28.86	22.8	41.2

30 **Table 2: Concentration of active substance according to the invention, on hairs on D 261.**

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DOG	CONCENTRATION ($\mu\text{g.g}^{-1}$)				
No.	UNDER THE COLLAR	RIGHT FLANK	LEFT FLANK	MIDDLE OF BACK	LUMBAR REGION
GROUP B					
363	0.94	0.65	>0.29	>0.39	1.47
87	0.64	0.94	>0.32	>0.40	ND
256	>0.97	ND	0.81	0.78	0.69
GROUP C					
289	3.16	>0.75	>0.59	>0.60	2.03
300	3.79	>0.70	2.04	1.35	5.52
335	1.84	1.67	2.99	4.61	4.19

ND = Not determined.

A distribution of active substance over the hair is observed: the concentrations on the different areas are higher with the formulation of Group C and are relatively homogeneous from one area to another.

The concentrations of active substance are still detectable 16 weeks after the collar has been taken off and are still effective at that stage.

Tables 3, 4 and 5 make it possible to carry out a concentration/activity correlation.

Table 3: Concentration/activity relationship on D 149.

DOG No.	CONCENTRATION ($\mu\text{g.g}^{-1}$)			ACTIVITY ⁽¹⁾	
	UNDER THE COLLAR	BACK AND FLANKS			FLEAS TICKS
		AV.	MIN	MAX	
5 GROUP B 363	559.5	15.6	10.7	24.8	0 1
10 GROUP C 289	871.3	48.9	30.8	94.4	0 0

(1) Number of fleas and ticks present on the dog

Table 4: Concentration/activity relationship on D 205.

DOG No.	CONCENTRATION ($\mu\text{g.g}^{-1}$)			ACTIVITY ⁽¹⁾	
	UNDER THE COLLAR	BACK AND FLANKS			FLEAS TICKS
		AV.	MIN	MAX	
20 GROUP B 363	18.6	3.54	1.73	6.99	0 12
	87	3.93	2.28	5.81	0 22
	256	4.88	2.48	11.0	0 15
25 GROUP C 289	27.5	16.7	8.99	30.9	0 12
	300	26.3	15.7	36.7	0 0
	335	29.2	22.8	41.2	0 0

(1): Number of fleas and ticks present on the dog

Table 5: Concentration/activity relationship on D 261.

DOG No.	CONCENTRATION ($\mu\text{g.g}^{-1}$)				ACTIVITY ⁽¹⁾	
	UNDER THE COLLAR	BACK AND FLANKS			FLEAS	TICKS
		AV.	MIN	MAX		
GROUP B						
363	0.94	>0.70	>0.29	1.47	0	21
87	0.64	<0.55	<LOQ	0.94	0	12
256	>0.97	<0.76	<LOQ	0.81	1	24
GROUP C						
289	3.16	>0.99	>0.59	2.03	0	28
300	3.79	>2.40	>0.70	5.52	0	19
335	1.84	3.37	1.67	4.61	0	3

(1): Number of fleas and ticks present on the dog

AV. = average

MIN = minimum

MAX = maximum

LOQ = limit of quantification = 0.25 $\mu\text{g/g}$

On D 261, the activity towards fleas is 100% on all the dogs, except for one dog (presence of a flea).

The minimum concentrations (on the hair) which are effective towards fleas and ticks are determined to be about:

- 20 micrograms per gram of hair for ticks

- 1 microgram per gram of hair for fleas.

An activity of at least 5 months for ticks and of at least 9 months for fleas is observed with these formulations.

EXAMPLE 2:

Dogs were divided up into 6 groups of 8 dogs:

- A: Control group: collar containing no active

substance.

- B: Reference product: commercial collar against fleas and ticks, containing 8% Chlorpyrifos (O,O-diethyl-O-(3,5,6-trichloro-2-pyridyl)phosphorothioate), referred to as ref. in the tables.

- C: Collar containing 2.5% compound A.

- D: Collar containing 5% compound A.

- E: Collar containing 10% compound A.

The collars were made with the same ingredients as in formulation 2 of Example 1, with, in addition, a pigment (titanium dioxide).

The tests follow the following schedule:

- 2 Infestation with fleas and ticks
- 0 Collars are put on
- 2 Counting with a comb
- 7 Reinfestation with ticks
- 8 Reinfestation with fleas
- 9 Counting with a comb
- 35 Reinfestation with ticks
- 36 Reinfestation with fleas
- 37 Counting with a comb

The process is continued along these lines from month to month.

Infestations and reinfestations are carried out at a rate of:

100 ± 10 fleas

50 ± 3 ticks

Tables 6 and 7 give the average effectiveness results.

Table 6: Percentage effectiveness on fleas, calculated as a geometric mean

DAY	GROUPS TREATED			
	Ref. 8%	2.5%	5%	10%
-5	0.0%	9.3%	0.0%	0.0%
2	63.9%	98.7%	100.0%	100.0%
5 9	96.3%	100.0%	100.0%	100.0%
37	96.1%	99.9%	100.0%	100.0%
65	99.1%	100.0%	100.0%	100.0%
93	99.6%	100.0%	100.0%	100.0%
121	99.4%	100.0%	100.0%	100.0%
10 149	98.3%	100.0%	100.0%	100.0%
177	97.9%	100.0%	100.0%	100.0%
205	98.5%	100.0%	100.0%	100.0%
233	96.6%	100.0%	100.0%	100.0%
268	89.6%	100.0%	100.0%	100.0%
15 289	68.4%	100.0%	100.0%	100.0%
317	76.0%	100.0%	100.0%	100.0%
345	79.5%	100.0%	100.0%	100.0%
373	-	100.0%	100.0%	100.0%
401	-	99.4%	100.0%	99.8%
20 429	-	99.2%	99.8%	99.3%
457	-	96.9%	98.8%	99.2%
485	-	96.7%	98.2%	98.7%
513	-	90.3%	99.0%	99.3%
541	-	-	98.8%	100.0%
25				

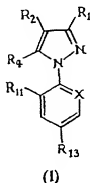
Table 7: Percentage effectiveness on ticks, calculated as a geometric mean

5	DAY	GROUPS TREATED			
		Ref. 8%	2.5%	5%	10%
	-5	4.7%	19.1%	19.1%	32.0%
	2	34.5%	67.0%	100.0%	98.5%
	9	86.9%	96.2%	100.0%	100.0%
	37	0.0%	27.2%	95.4%	95.4%
10	65	31.7%	85.0%	100.0%	95.8%
	93	31.8%	86.7%	100.0%	95.7%
	121	65.2%	91.3%	88.8%	92.1%
	149	59.0%	93.4%	92.0%	94.5%
	177	67.2%	84.9%	95.3%	95.2%
15	205	62.0%	86.2%	100.0%	98.4%
	233	62.6%	89.8%	98.3%	97.9%
	268	57.5%	77.4%	98.2%	99.5%
	289	44.6%	92.4%	97.2%	95.1%
	317	-	74.5%	85.6%	92.4%
20	345	-	88.1%	98.8%	98.0%
	373	-	72.4%	93.9%	95.7%
	401	-	63.4%	98.5%	93.6%
	429	-	75.3%	83.2%	93.3%
	457	-	62.4%	84.1%	86.7%
25	485	-	-	-	-
	513	-	-	-	-
	541	-	-	-	-

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CLAIMS

1. Anti-flea and anti-tick collar or other external device for a pet, in particular a cat or dog, made of a matrix in which is incorporated from 0.1 to 40% by weight, relative to the collar, of a substance which is active against fleas and ticks, this active substance being formed of at least one compound corresponding to formula (I) below:



in which:

R_1 is CN or methyl or a halogen atom;

R_2 is $S(O)_nR_3$ or 4,5-dicyanoimidazol-2-yl or haloalkyl;

R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical NR_5R_6 , $S(O)_mR_7$, $C(O)R_7$, $C(O)O-R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)(R_{10})$;

R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, $C(O)alkyl$, alkoxy carbonyl or $S(O)_tCF_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

R₇ represents an alkyl or haloalkyl radical;

R₈ represents an alkyl or haloalkyl radical or a hydrogen atom;

R₉ represents an alkyl radical or a hydrogen atom;

5 R₁₀ represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

R₁₁ and R₁₂ represent, independently of each other, a hydrogen or halogen atom, or CN or NO₂;

10 R₁₃ represents a halogen atom or a haloalkyl, haloalkoxy, S(O)_qCF₃ or SF₅ group;

m, n, q and r represent, independently of each other, an integer equal to 0, 1 or 2;

15 X represents a trivalent nitrogen atom or a radical C-R₁₂, the other three valency positions of the carbon atom forming part of the aromatic ring;

20 with the proviso that when R₁ is methyl, either R₃ is haloalkyl, R₄ is NH₂, R₁₁ is Cl, R₁₃ is CF₃ and X is N; or R₂ is 4,5-dicyanoimidazol-2-yl, R₄ is Cl, R₁₁ is Cl, R₁₃ is CF₃ and X is =C-Cl;

25 this collar or other external device being designed to ensure more than 6 months of efficacy against fleas and more than 3 months of efficacy against ticks, the efficacy preferably being maintained for several weeks even if the collar or other external device is taken off or lost or if there is a variation in the release of the compound (I) by the matrix.

2. Collar according to claim 1, characterized in that the compound of formula (I) is such that:

30 R₁ is CN or methyl;

R₂ is S(O)_nR₃;

R₃ is alkyl or haloalkyl;

R₄ represents a hydrogen or halogen atom; or a

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radical NR_5R_6 , $\text{S(O)}_n\text{R}_7$, $\text{C(O)}\text{R}_7$, alkyl, haloalkyl or OR_8 or a radical $-\text{N}=\text{C}(\text{R}_9)(\text{R}_{10})$;

5 R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, $\text{C(O)}\text{alkyl}$ or $\text{S(O)}_n\text{CF}_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

R_7 represents an alkyl or haloalkyl radical;

10 R_8 represents an alkyl or haloalkyl radical or a hydrogen atom;

R_9 represents an alkyl radical or a hydrogen atom;

R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

15 R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom;

R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, $\text{S(O)}_n\text{CF}_3$ or SF_5 group;

20 m , n , q and r represent, independently of each other, an integer equal to 0, 1 or 2;

X represents a trivalent nitrogen atom or a radical C-R_{12} , the other three valency positions of the carbon atom forming part of the aromatic ring;

25 with the proviso that when R_1 is methyl, then R_3 is haloalkyl, R_4 is NH_2 , R_{11} is Cl, R_{13} is CF_3 and X is N.

3. Collar according to claim 2, wherein the compound of formula (I) is such that R_1 is CN.

4. Collar according to claim 2, wherein the compound of formula (I) is such that R_{13} is haloalkyl.

30 5. Collar according to claim 4, wherein the compound of formula (I) is such that R_{13} is CF_3 .

6. Collar according to claim 2, wherein the compound of formula (I) is such that R_2 is $\text{S(O)}_n\text{R}_3$.

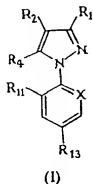
7. Collar according to claim 6, wherein $n = 1$ and R_3 is chosen among the group consisting of CF_3 , methyl, ethyl.
8. Collar according to claim 6, wherein $n = 0$ and R_3 is CF_3 .
9. Collar according to claim 2, wherein the compound of formula (I) is such that X is $C-R_{12}$, R_{12} being a halogen atom.
10. Collar according to claim 2, wherein the compound of formula (I) is chosen from those in which R_1 is CN, R_3 is haloalkyl, R_4 is NH_2 , R_{11} and R_{12} are, independently of each other, a halogen atom, and/or R_{13} is haloalkyl.
11. Collar according to claim 2, wherein the compound of formula (I) is chosen among the group consisting of compound A:
 $1-[2,6-Cl_2-4-CF_3phenyl]3-CN4-[SO-CF_3]5-NH_2pyrazole$
and its derivatives with $n=0$ and R_3 is CF_3 , and $n=1$ and R_3 is ethyl.
12. Collar according to claim 2, wherein the collar comprises from 1 to 15% active substance.
12. Collar according to claim 2, wherein the collar comprises from 1.25 to 10% active substance.
13. Collar according to claim 2, wherein the collar comprises from 2 to 6% active substance.
14. Collar according to claim 2, wherein the collar comprises from 2.5 to 5% active substance.
15. Collar according to claim 11, wherein the collar comprises from 1.25 to 10% active substance.
16. Collar according to claim 11, wherein the collar comprises from 2 to 6% active substance.
17. Collar according to claim 11, wherein the collar comprises from 2.5 to 5% active substance.

18. Collar according to claim 11, wherein the efficacy is maintained when the collar or external device is taken off or lost, over a period ranging from 2 to 3 months against fleas and from 1 to 2 months against ticks.

19. Collar according to claim 11, wherein it comprises a concentration of active substance which ensures effective protection against fleas for a period longer than or equal to 12 or 18 months.

20. Collar according to claim 11, wherein it comprises a concentration of active substance which ensures effective protection against ticks for a period longer than or equal to 12 or 15 months.

21. Method for eliminating fleas and ticks from pets, in particular cats and dogs, in which one attaches to the pets at least one collar or other external device which comprises a compound corresponding to formula (I) below:



in which:

R_1 is CN or methyl or a halogen atom;

R_2 is $S(O)_2R_3$ or 4,5-dicyanoimidazol-2-yl or haloalkyl;

R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical NR_5R_6 , $S(O)_mR_7$, $C(O)R_7$, $C(O)O-R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)(R_{10})$;

5 R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, $C(O)$ alkyl, alkoxycarbonyl or $S(O)_rCF_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

10 R_7 represents an alkyl or haloalkyl radical;

R_8 represents an alkyl or haloalkyl radical or a hydrogen atom;

R_9 represents an alkyl radical or a hydrogen atom;

15 R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom, or optionally CN or NO_2 ;

20 R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, $S(O)_qCF_3$ or SF_5 group;

m, n, q and r represent, independently of each other, an integer equal to 0, 1 or 2;

25 X represents a trivalent nitrogen atom or a radical $C-R_{12}$, the other three valency positions of the carbon atom forming part of the aromatic ring;

with the proviso that when R_1 is methyl, either R_3 is haloalkyl, R_4 is NH_2 , R_{11} is Cl, R_{13} is CF_3 and X is N; or R_2 is 4,5-dicyanoimidazol-2-yl, R_4 is Cl, R_{11} is Cl, R_{13} is CF_3 and X is $=C-Cl$;

30 which method ensuring prevention and treating fleas and ticks to a high degree of efficacy and over a period exceeding 6 months against fleas and 3 months against ticks, the efficacy preferably being maintained over

several weeks even if the collar or external device is taken off or if there is a variation in the release of the compound (I) by the collar or external device.

22. Method according to claim 21, wherein the compound of formula (I) is such that:

R_1 is CN or methyl;

R_2 is $S(O)_n R_3$;

R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical $NR_5 R_6$, $S(O)_m R_7$, $C(O)R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)(R_{10})$;

R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, $C(O)alkyl$ or $S(O)_2 CF_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms, such as oxygen or sulphur;

R_7 represents an alkyl or haloalkyl radical;

R_8 represents an alkyl or haloalkyl radical or a hydrogen atom;

R_9 represents an alkyl radical or a hydrogen atom;

R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, -S-alkyl, cyano or alkyl;

R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom;

R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, $S(O)_q CF_3$ or SF_5 group;

m, n, q and r represent, independently of each other, an integer equal to 0, 1 or 2;

X represents a trivalent nitrogen atom or a radical $C-R_{12}$, the other three valency positions of the carbon atom forming part of the aromatic ring;

with the proviso that when R_1 is methyl, then R_3 is

haloalkyl, R_4 is NH_2 , R_{11} is Cl, R_{13} is CF_3 and X is N.

23. Method according to claim 22, wherein the compound of formula (I) is such that R_1 is CN.

24. Method according to claim 22, wherein the compound of formula (I) is such that R_{13} is haloalkyl.

25. Method according to claim 22, wherein the compound of formula (I) is such that R_{13} is CF_3 .

26. Method according to claims 22, wherein the compound of formula (I) is such that R_2 is $S(O)_nR_3$.

27. Method according to claim 26, wherein $n = 1$ and R_3 is chosen among the group consisting of CF_3 , methyl, ethyl.

28. Method according to claim 26, wherein $n = 0$ and R_3 is CF_3 .

29. Method according to claim 22, wherein the compound of formula (I) is such that X is $C-R_{12}$, R_{12} being a halogen atom.

30. Method according to claim 22, wherein the compound of formula (I) is such that R_1 is CN, R_3 is haloalkyl, R_4 is NH_2 , R_{11} and R_{12} are, independently of each other, a halogen atom, and/or R_{13} is haloalkyl.

31. Method according to claim 22, wherein the compound of formula (I) is chosen among the group consisting of compound A:

1-[2,6-Cl₂4- CF_3 phenyl]3-CN4-[SO- CF_3]5- NH_2 pyrazole and its derivatives with $n=0$ and R_3 is CF_3 , and $n=1$ and R_3 is ethyl.

32. Method according to claim 22, wherein the compound of formula (I) is present in a proportion of from 1 to 15% by weight.

33. Method according to claim 22, wherein the compound of formula (I) is present in a proportion of from 1.25 to 10%.

34. Method according to claim 22, wherein the compound of formula (I) is present in a proportion of from 2 to 6%.
35. Method according to claim 22, wherein the compound of formula (I) is present in a proportion of from 2.5 to 5% by weight.
36. Method according to claim 31, wherein the compound of formula (I) is present in a proportion of from 1.25 to 10%.
37. Method according to claim 31, wherein the compound of formula (I) is present in a proportion of from 2 to 6% by weight.
38. Method according to claim 31, wherein the compound of formula (I) is present in a proportion of from 2.5 to 5% by weight.
39. Method according to claim 31, wherein the efficacy is greater than 95% against fleas.
40. Method according to claim 31, wherein the efficacy is greater than 98% or 99% against fleas.
41. Method according to claim 31, wherein the efficacy is greater than 80% against ticks.
42. Method according to claim 31, wherein the efficacy is greater than 90% against ticks.
43. Method according to claim 31, wherein the long-lasting efficacy is longer than or equal to 12 months against fleas.
44. Method according to claim 31, wherein the long-lasting efficacy is longer than or equal to 18 months against fleas.
45. Method according to claim 31, wherein the long-lasting efficacy is longer than or equal to 12 months against ticks.
46. Method according to claim 31, wherein the long-

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lasting efficacy is longer than or equal to 15 months against ticks.

47. Method according to claim 31, wherein the efficacy is maintained when the collar or external device is taken off or lost, over a period ranging from 2 to 3 months against fleas and from 1 to 2 months against ticks.

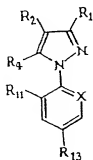
09174598.101998

COMPANY KNOWN AS: RHONE MERIEUX

**N-Phenylpyrazole-based anti-flea and anti-tick collar
for cats and dogs**

ABSTRACT

Collar or other external device for a pet, in particular a cat or dog, made of a matrix in which is incorporated from 0.1 to 40% by weight, preferably from 1 to 15 % by weight, relative to the collar, of a substance which is active against ectoparasites such as fleas and ticks, this active substance being formed of at least one compound corresponding to formula (I) below:



(I)

this collar or other external device being designed to ensure more than 6 months of efficacy against fleas and more than 3 months of efficacy against ticks, the efficacy being maintained for several weeks even if the collar or other external device is taken off or lost or if there is a variation in the release of the compound.

09174598-101598

DECLARATION FOR USA PATENT APPLICATION

(including Design and National Stage PCT)

Attorney's Docket ID: XL/P03139US1

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below adjacent to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled N-PHENYLPYRAZOLE-BASED ANTI-FLEA AND ANTI-TICK COLLAR FOR CATS AND DOGS

the specification of which is attached hereto. (or)

X was filed on May 27, 1997, [] and was amended on _____

[X] as U.S. Application No. 08/863,182 or

[] as International PCT Application No. _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 (a) - (d) or § 365 (b) of any foreign application(s) for patent or inventor's certificate, or § 365 (a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below, where priority is not claimed, any foreign application for patent or inventor's certificate, or any PCT International application, having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s) () ADDITIONAL APPLICATIONS IDENTIFIED ON ATTACHED SHEET:

Number	Country	Day/Month/Year Filed	Priority Not Claimed
<u>96 04 206</u>	<u>FRANCE</u>	<u>29 March 1996</u>	<u> </u>
<u>97 03 707</u>	<u>FRANCE</u>	<u>26 March 1997</u>	<u> </u>

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s), or § 365 (c) of any PCT International application designating the U.S., listed below; and insofar as the subject matter of each claim of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application. () ADDITIONAL APPLICATIONS IDENTIFIED ON ATTACHED SHEET:

Application Serial No.	Day/Month/Year Filed	Status -- patented, pending, abandoned
<u>08/692,430</u>	<u>5 August 1996</u>	<u>Abandoned</u>

I hereby appoint the practitioners of LARSON & TAYLOR associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number.

CUSTOMER NUMBER: 00881

Direct all telephone calls to Thomas P. Sarro, at TEL (703) 739-4900 (Fax: 703-739-9577)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of Sole Inventor	<u>Philippe JEANNIN</u>	Citizenship	<u>FRANCE</u>
Full Post Office Address	<u>104 chemin de la Peyrette - 31170 TOURNEFEUILLE, FRANCE</u>		
Residence - City, State/Country (if different from P.O. address)			
SIGN AND DATE HERE: Inventor's Signature:	<u>Philippe Jeannin</u>	Date:	<u>24-11-97</u>
Full Name of Second Joint Inventor, if any		Citizenship	
Full Post Office Address			
Residence - City, State/Country (if different from P.O. address)			
SIGN AND DATE HERE: Inventor's Signature:		Date:	
Full Name of Third Joint Inventor, if any		Citizenship	
Full Post Office Address			
Residence - City, State/Country (if different from P.O. address)			
SIGN AND DATE HERE: Inventor's Signature:		Date:	
Full Name of Fourth Joint Inventor, if any		Citizenship	
Full Post Office Address			
Residence - City, State/Country (if different from P.O. address)			
SIGN AND DATE HERE: Inventor's Signature:		Date:	

SEE ATTACHED SHEET FOR SIMILAR INFORMATION AND SIGNATURE FOR ADDITIONAL JOINT INVENTORS.
LARSON & TAYLOR, 1199 North Fairfax Street, Suite 900, Alexandria Virginia 22314

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney's Docket: XI/P03139US2

In re application of:

JEANNIN, Philippe

Divisional Application of

Serial No. 08/863,182

: Art Unit: 1615

Filed: Concurrently herewith

: Examiner: N. Levy

For: N-PHENYLPYRAZOLE-BASED ANTI-FLEA AND ANTI-TICK COLLAR FOR CATS
AND DOGS

CUSTOMER NUMBER and CHANGE OF ADDRESS

Honorable Assistant Commissioner of Patents

Washington, D. C.

S I R:

Please change the address of LARSON & TAYLOR to:

LARSON & TAYLOR

Suite 900

1199 North Fairfax Street

Alexandria, Virginia, 22314

The address is associated with the Customer Number provided below. Direct all
correspondence to the Customer Number for the above-identified patent application.

CUSTOMER NUMBER: 000881

Respectfully submitted,

LARSON & TAYLOR

Date: October 19, 1998



Thomas P. Sarro
Registration No. 19,396